REMARKS

Claims 1, 4, 7, 8, 11-14, 20, 21, 23-27, 29-32, 37-41 and 51-59 are in the application. Claims 1 and 21 have been amended

Rejection under 35 USC §103

Claims 1, 4, 7, 11-14. 20-21, 23-25, 27, 29-32, 37-41 and 51-59 stand rejected under 35 USC §103(a) as being unpatentable over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190). Applicants respectfully traverse this rejection.

Claims 8 and 26 stand rejected under 35 USC §103(a) as being unpatentable over Breitenbach et al. (US 6,150,424) in view of Jane et al. (US 5,710,190) and De Bock et al. (US 5, 428, 150). Applicants also respectfully traverse this rejection.

Applicants two independent claims, Claim 1 and Claim 21 have been amended to recite the language 'consisting of' instead of 'comprising', thus removing the Examiners argument that the claims while not affirmatively reciting inclusion of a thermoplastic polymer could include such. Thus, Claim 1 and Claim 21 as amended are believed to render this objection moot.

As previously noted, the Breitenbach et al. patent is directed to a tablet which comprises as the foaming polymer, a thermoplastic polymer selected from a water-soluble, melt processable homo- or co-polymer of N-vinylpyrrolidone or mixtures of such polymers (see Column 2, lines 58-60).

The claimed invention herein is to be able to mimic the behavior of a thermoplastic polymer without the need for including such a polymer in a pharmaceutical composition. Claim 1 requires specific polyols and a non-thermosetting modifier and/or non-thermosetting polymer. In direct contrast to this, the Breitenbach et al. patent requires a thermoplastic polymer, such as N-vinylpyrrolidone. Applicants have further amended claim 1, in order to advance prosecution on the merits to include in the closing body of the claim "molded microcellular" to clarify that in fact this is the dosage form

achieved and the more limiting language of "consisting of" should further distinguish Applicants claimed invention over the Breitenbach et al. patent. Claim 1 also includes the phrase 'single phase homogenous mixture" and claim 21 has been amended to add the term "single phase" to the term "homogenous mixture" already present. Support for this is found through out the specification, such as on page 8 and in the claims as filed.

The claims of the present invention clearly do not use a thermoplastic polymer. The reference does not teach that "all of the claimed elements are found in Breitenbach and Jane" (See Office Action, page 4, 1rst full ¶). There is no basis to start with the teachings of Breitenbach and remove the primary polymer and replace it with the teachings of the secondary reference of Jane, absent an improper hindsight rejection.

Furthermore, the teachings of Jane et al. would still not does not remedy the lack of teachings in the Breitenbach et al reference. Jane et al. discloses a thermoplastic composition based upon a soy protein. Applicants do not use nor require a thermoplastic polymer to achieve the molded dosage form. The Jane reference fails to supply the necessary motivation to direct the skilled artisan to modify the teachings of the Breitenbach et al. patent to achieve the invention as claimed herein. There is no disclosure in Breitenbach alone or taken with the Jane reference that teaches the specific combination of a polyol and the non-thermoplastic polymer or modifier as the matrix of the resulting tablet.

The Examiner references the KSR case as saying that "one of ordinary skill in the art could have combined the elements and the combination would have yielded predictable results" (See Office Action, page 4, 1rst full ¶). This is however quite wrong.

There is no 'mere substitution of one element for another" which is known in this filed. This is not merely a substitution of one thermoplastic polymer, e.g. a homo- or co-polymer of N-vinylpyrrolidone for another thermoplastic, in this instance, a soy protein polymer. This is using a completely different class of polymers, a non-thermosetting polymerized material comprised of at least one polyol selected from lactitol, xylitol, erythritol, sorbitol, maltitol, or mannitol, or combinations thereof; and at least one of

a) a non-thermosetting modifier selected from a starch, maltodextrin, a dextrose equivalent, polyalditol, a hydrogenated starch hydrosylate, or a mixture thereof; and/or

b) a non-thermosetting polymer selected from carboxymethyl cellulose sodium, methyl cellulose, ethylcellulose, hydroxyethylcellulose (HEC), hydroxypropylmethyl cellulose (HPMC), hydroxypropylmethyl cellulose phthalate, cellulose acetate phthalate, noncrystalline cellulose, starch and its derivatives, and sodium starch glycolate or mixtures thereof.

The principles underlining a KSR analysis allows an Applicant to challenge an obviousness rejection based upon a combination of elements in the prior art by a number of factors, including whether there was even a problem to solve. There is no discussion or suggestion in either the Breitenbach or the Jane et al. article that there is a need or in fact a problem remaining to be solved that either or both of the patents didn't achieve.

Injection molding has never been successful for pharmaceutical tablets, and most tablets are still produced by tablet presses. Breitenbach is one attempt to extrude tablets, but Breitenbach does not produce a molded microcellular dosage form. Breitenbach's simple mixtures do not (and cannot) attain the same degree of microcellular foam structure as required by the claims of the present invention, such as recited in Claim 21, specifically. Breitenbach used a traditional thermoplastic polymer in a melt extrusion process. There are a number of traditional thermoplastic polymer available, but they are "finite, and identifiable". This is in contrast to Applicants invention which is to attempt to mimic the qualities that thermoplastic polymers have and to take advantage of injection molding and extrusion processes to produce high quality solid dosage forms that have conventional, time release, or flash-dispersal solution characteristics, and to produce these dosage forms at low cost by forming them continuously over a long time without interruption.

The microcellular structure of the dosage form achieved by Applicants not only ensures good control but also enables the manufacturer to maintain very close tolerances in the process. The microcellular internal configuration contributes to rapid dissolution of the tablet, and at the same time producing a tablet that has sufficient resistance to breaking up during handling. This allows a flash-dispersal tablet to be supplied in a

conventional bottle rather than in blister packages. Such a benefit it not shown nor suggested by either of the references.

If the desire is to substitute the thermoplastic polymer of Breitenbach for another excipient, there would be many possibilities to consider, and only one of those choices might be the thermoplastic polymer of Jane. To completely withdraw the thermoplastic polymer and substitute not one but two excipients for the same polymer is most unlikely. There is no direction to use the combination of elements chosen by Applicants to achieve the effect which they have shown herein.

One of ordinary here is no "proposed modification of the applied reference" under any circumstance that could be used to arrive at Applicants claimed subject matter. There is "no proposed modification of the applied reference" taken with any of the secondary references, under any circumstances, that could be used to arrive at Applicants claimed subject matter.

The explanation provided by the Examiner is simply that Breitenbach et al. optionally includes some of the excipients defined as a non-thermosetting modifier herein. Even if these additional excipients are added, the formulation still does not achieve what teach and claim.

Breitenbach prepares an expanded extrudate, and that these extrudates then have to undergo a secondary processing step to be turned into pharmaceutical dosage forms. Looking at column 5, lines 2-5: "The foamed active ingredient preparation is subsequently shaped to the required active ingredient forms in each case, for example by pelleting, granulating or tableting by known processes."

In contrast, Applicant's form a foamed "active ingredient form" in-situ in the mold cavity, by injection molding. This is by first intent, it is in a single process not two! Extrusion and injection molding are fundamentally two different processes.

Applicants process is unique relative to Breitenbach's. The present invention utilizes supercritical N_2 or CO_2 injection, which dissolves in the melted mass in the high pressure environment of the injection molder screw to form a single phase material.

Breitenbach on the other hand uses a relatively low pressure twin screw extruder, and with their simple mixture cannot attain the same degrees of microcellular foam structure that Applicants can. While claim 21 has already contained the requirement of "homogenous", insertion of the 'single-phase" is now added thereto as well. These limitations are not taught in Breitenbach nor in the combination of the references.

The present invention is the novel combination of agents which when prepared in a manner as described in the specification produce a microcellular foamed tablet containing an active pharmaceutical agent.

As previously discussed, there is a significant difference between the present invention and the Breitenbach et al. disclosure in that the microcellular foam tablets of the present invention are formed in-situ, by first intent, in a novel injection molding process. Breitenbach et al. prepares thermoplastic foam extrudates in a conventional extruder. The extrudates are then shaped into forms by secondary processes, i.e., cutting, chopping, punching (see column 5, lines 31 to 61). Consequently, the formulation and the process of using this formulation to make injection molded tablets will be, and is, fundamentally different. What reason exists to make the necessary modifications to the formulation if the use of that formulation is different?

The Examiner comments that Applicants arguments with respect to Claim 21 are not persuasive as Breitenbach teaches a solid, foamed active ingredient preparation. Solid is not the same as rigid, and having particular **microcellular** characteristics. Breitenbach fails to recite the specific claim limitations.

The Breintenbach et al. polymers are classic polymeric thermoplastic materials. In contrast, the presently claimed invention employs the novel use of thermosetting agents, such as polyols in combination with one or both of a non-thermosetting modifier and a non-thermosetting polymer. The non-thermosetting modifiers are selected from starch, maltodextrin, a dextrose equivalent, polyalditol, or a hydrogenated starch hydrosylate, or mixtures thereof.

The non-thermosetting polymers are selected from carboxymethyl cellulose sodium, methyl cellulose, ethylcellulose, hydroxyethylcellulose (HEC), hydroxypropylmethyl cellulose (HPMC), hydroxypropylmethyl cellulose phthalate, cellulose acetate phthalate, noncrystalline cellulose, starch and its derivatives, and sodium starch glycolate or mixtures thereof.

The fact that you can produce a composition that can be injection molded into foamed tablets **despite the fact they are not thermoplastic** is an **unexpected and a novel invention.**

This novelty is not taught nor disclosed by the prior art.

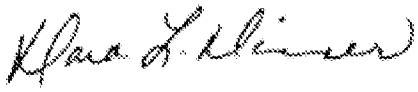
The Examiner uses another secondary reference, De Bock et al. (US 5, 428, 150) to teach a starch based formulation which can be **extruded,** but not injection molded, as required by amended Claim 1. There is no disclosure of this composition being used with a supercritical fluid to form a microcellular foam product. The only disclosure is to combine the composition with a thermoplastic polymeric material (column 5, lines 9-13). This is an improper hindsight rejection to maintain that the skilled artisan would know to substitute a starch based formulation in the composition of Breitenbach and know that such formulation could be injection molded under supercritical fluid conditions to achieve a closed cell foam with microcellular characteristics.

In view of these remarks and amendments, reconsideration and withdrawal of the rejection to the claims under 35 USC §103 is respectfully requested.

CONCLUSION

Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. If any additional fees or charges are required by this paper the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,



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